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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/671,953	09/27/2000	Claude Meares	2307O-099120US	8313

20350 7590 05/24/2004

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EXAMINER	
HELMS, LARRY RONALD	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 05/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/671,953	MEARES ET AL.	
	Examiner	Art Unit	
	Larry R. Helms	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 March 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,10,11,14-25,30-38 and 42-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *10 and 11* is/are allowed.

6)☒ Claim(s) *1-3, 14, 16-25, 30-38, 42-44* is/are rejected.

7)☒ Claim(s) *15* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1, 15, 17, 21, 31, have been amended.

2. Claims 1-3, 10-11, 14-25, 30-38, 42-44 are under examination.

3. The text of those sections of Title 35 U.S.C. code not included in this office action can be found in a prior Office Action.

Rejection Withdrawn

4. The rejection of claims 1-3, 16, 17, 18, 19, 20, 22, 23, 24, 25, 30, 31, 32, 33, 34, 37, 38, 42, and 44 under 35 U.S.C. 103(a) as being unpatentable over Reardan et al (Nature 316:265-267, 1985, IDS #7) and further in view of Orlandi et al (Proc. Natl. Acad. Sci. USA 86:3833-3837, 1989) and Pastan et al (U.S. Patent 5,747,654, issued 5/5/98, IDS #8) and Goodwin et al (The Journal of nuclear medicine 29:226-234, 1988, IDS #7) is withdrawn in view of the amendments to the claims.

5. The rejection of claim 15 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of the amendment to the claim.

6. The rejection of claim 15 under 35 U.S.C. 112, first paragraph, is withdrawn in view of the amendment to the claim.

Response to Arguments

7. The rejection of claim 44 under 35 U.S.C. § 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with

which it is most nearly connected, to use the invention, because the specification does not provide evidence that the claimed biological materials are (1) known and readily available to the public; (2) reproducible from the written description is maintained.

The response filed 3/1/04 has been carefully considered but is deemed not to be persuasive. The response states that the specification supplies ample guidance to make the claimed antibodies and the declaration of Dr. Meares explains that the specification describes multiple methods for generating the mutant antibodies and the specification provides two working examples of mutant CHA255 antibodies (see page 9-10 of response). The declaration of Dr. Meares has been carefully considered but is deemed not to be persuasive. While the specification may provide two example of mutant CHA255 antibodies, the CHA255 antibody is needed to practice the invention. Therefore a deposit is required as stated in the rejection. The deposit has not been made and the rejection is maintained.

8. The rejection of claims 1-3, 16-19, 24, 42, 44 under 35 U.S.C. 102(b) as being anticipated by Stickney et al (Cancer Research 51:6650-6655, 1991, IDS #7) is maintained.

The response filed 3/1/04 has been carefully considered but is deemed not to be persuasive. The response states that as defined by the specification and explained in the declaration of Dr. Meares, a mutation is a substitution, addition, or a deletion in a nucleotide encoding a polypeptide (see page 23, lines 26-28 in the specification and declaration paragraph 5) and the antibody of Strickney et al is generated by chemically

linking the binding sites of two separate antibodies (see page 11 of response). In response to this argument, the declaration of Dr. Meares has been carefully considured but is deemed not to be persuasive. The specification does not limit a "mutation" as that defined on page 23 of the specification. There is nothing limiting this in the claims and in fact the specification discloses that "The mutant antibodies are prepared by any method known in the art" (see page 23, line 16) and as such a "mutant" antibody is provided by the art of Strickney. Stickney et al does describe a mutant antibody because the (Fab')2 is made by combining the binding sites of two separate antibodies to create a mutant antibody. In addition, the addition of the linker would broadly be a mutation wherein a mutation can be a chemical alteration of the protein or addition of a linker and the linker does have a reactive site that can interact with carboxyl groups as stated previously because the linker is a bis-maleimidomethyl ether and the linker would be a reactive site for acids, for example. The claims require a reactive site and the art of Stickney teach a linker with a reactive site.

9. The rejection of claim 43 under 35 U.S.C. 103(a) as being unpatentable over Reardan et al (Nature 316:265-267, 1985, IDS #7) and further in view of Orlandi et al (Proc. Natl. Acad. Sci. USA 86:3833-3837, 1989) and Pastan et al (U.S. Patent 5,747,654, issued 5/5/98, IDS #8) and Goodwin et al (The Journal of nuclear medicine 29:226-234, 1988, IDS #7) is maintained.

The response filed 3/1/04 has been carefully considured but is deemed not to be persuasive. The response states that the combination of references fails to disclose

each element of the claimed invention and the response then addresses each reference (see page 12-16 of response). The response states that the claims have been amended for clarity to recite that the reactive site reacts with a reactive group on the metal chelate (see page 16 of response). In response to this argument, claim 43 does not recite such a limitation and as such the rejection is maintained for this claim because Pastan et al clearly teaches a disulfide stabilized antibody and the antibody comprises a SH group not present in the wildtype antibody. The claims require a "reactive site" and the disulfide stabilized antibody has a reactive group because the disulfide bond would react with a reducing agent or reacts with another SH which was added in the method of Paston. With regard to Goodwin et al Goodwin et al clearly teaches a chelate comprising a reactive functional group of complementary reactivity to the reactive site (see figure 1). It would have been obvious to produce the claimed invention because Pastan et al teaches the antibodies can be stabilized for greater stability and have small size and reach there target more rapidly and cleared quicker for targeting and imaging application (see column 2, lines 49-55) and Goldwin et al antibody is used for imaging and it would have been obvious to stabilized Goodwin et al antibody by the method of Pastan et al for the reasons states by Pastan.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

10. The rejection of claims 1-3, 14, 16-25, 30-38, 42-44 under 35 U.S.C. 112, first paragraph, is maintained.

The response filed 3/1/04 has been carefully considered but is deemed not to be persuasive. The response states that the declaration of Dr. Meares explains that there is ample guidance for the full scope of the claimed invention of a mutant site proximate to or within a CDR and the specification provides actual working examples of generation of two CHA255 mutants the examples describe the generation of a mutant antibody using computer based design to choose a position for the reactive site proximate or within the CDR (see page 18-19 of response). In response to this argument, the declaration and response has been carefully considered but is deemed not to be persuasive. The examples are for mutants proximate to a CDR and not in a CDR. As stated in the rejection the prior art does not recognize mutations in a CDR and obtain a mutant that would still bind antigen. The prior art teaches that even one alteration lead to alteration in binding antigen. The claims require a mutation in the CDR and as such one skill in the art would not conclude that such a mutation could be made and maintain the required binding.

Conclusion

11. Claims 10 and 11 are in condition for allowance, claim 15 is objected to as depending on a rejected claim.

12. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (571) 272-0832. The examiner can normally be reached on Monday through Friday from 6:30 am to 4:00 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (571) 272-0871.

14. Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center telephone number is (703) 308-4242.

Respectfully,

Larry R. Helms Ph.D.

571-272-0832